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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,371	07/18/2003	Chia-Chann Shiue	Q76645	4052

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EXAMINER	
SNAY, JEFFREY R	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 06/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,371	SHIUE ET AL.	
	Examiner	Art Unit	
	Jeffrey R. Snay	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/18/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-10 and 19-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to o-phthalaldehyde as the fluorophor-producing reactant and either Tris-(hydroxymethyl) aminomethane (TRIS) or acetamide as the competing agent, does not reasonably provide enablement for the use of other compounds for such purposes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification clearly establishes the unpredictability associated with applicant's disclosed method. For example, utilization of TRIS in combination with 0-phthalaldehyde accomplishes clear differentiation between cysteine and homocysteine (Figure 2A). However, when either HEPES or phosphate is substituted for the TRIS buffer, "the fluorescence of cysteine can't be quenched." (Specification at column 10, lines 11-13).

Furthermore, when acetamide is substituted for TRIS as the competing agent, the specification teaches that an entirely different effect is observed. Whereas TRIS acts to preclude cysteine from forming a fluorescent reaction product, acetamide acts to

produce distinguishably different fluorescent products from cysteine and homocysteine, respectively. That is, use of acetamide as disclosed results in distinction between cysteine and homocysteine based on the different emission wavelengths of the two reaction products.

For the foregoing reasons, the specification makes clear that the presently disclosed method constitutes a specialized discovery in an unpredictable field. The only substitutions for the competing agent described by the specification result in the desired measurement being either impossible or obtained by an entirely different mechanism.

The specification fails to provide any guidance by which one of ordinary skill in the art would have been guided toward likely candidates for substitution. Based in the unpredictability of the disclosed method, as exemplified by applicant's own specification, such guidance would have been essential in order to enable any substitutions for the specifically taught reagents.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3, 5 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 indirectly limits parent claim 2 in an ambiguous manner. Specifically, claim 3 limits the amine compound while such amine compound is recited in parent

claim 2 as only a possible member from a group of alternatives. Thus, claim 3 is ambiguous as to whether or not the particular amine recited by claim 3 is positively required.

Claim 6 is indefinite because the limitation recited therein is at least partially precluded by parent claim 2. Specifically, parent claim 2 allows for the selection of acetamide as the competing agent. The specification teaches that acetamide fails to satisfy the condition recited in dependent claim 6.

Claim 23 is rejected for reasons analogous to those stated above with respect to claim 3. Specifically, claim 23 indirectly limits TRIS such that the claim is ambiguous as to whether or not TRIS is the required selection from the group of alternatives recited in parent claim 21.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-12, 14-22 and 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Ullman ('220).

Ullman discloses a method for measuring homocysteine in a biosample which includes all of the presently recited steps, as well as the presently recited kit

components. Specifically, Ullman teaches measuring homocysteine in a cysteine-containing serum or urine sample by adding o-phthalaldehyde as a reactive reagent (column 7, first paragraph) and measuring the resulting fluorescent emission (column 7, lines 45-50). Ullman further teach the addition of TRIS buffer (column 8, line 33), which anticipates the presently recited "competing agent." The reactive reagent is presented in a concentration of 1 to 100 mM (column 8, lines 50-53). Regarding present claims 8-10, it is noted that Ullman teaches reaction times ranging from 30 seconds to 5 minutes (column 9, first full paragraph), which appear to anticipate the presently recited operation times. Regarding instant claim 12, Ullman further teaches the incorporation of both EDTA and sodium borohydride (Example 1).

Regarding instant claim 14, see Ullman at example 1. Regarding instant claims 15-17, it is noted that Ullman teaches reaction times ranging from 30 seconds to 5 minutes (column 9, first full paragraph), which appear to anticipate the presently recited operation times.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 13 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman.

The method and kit of Ullman, as described above, differ from instant claims 13 and 23 in that it fails to specify the presently recited concentrations. However, whereas the TRIS concentration is presently claimes as 100 mM, Ullman teaches the alternative use of either TRIS or HEPES, and discloses the specific concentration of 100mM for HEPES (Example 1). It would have been obvious to one of ordinary skill in the art to utilize the same concentration for the disclosed equivalent, TRIS. With respect to the

presently claimed EDTA concentration of 1 mM, see Ullman at Example 1. With respect to the presently claimed borohydride concentraiton of about 18mM, Ullman teaches such concentration as 10 mM. However, the provision of borohydride is not central to the operation of the Ullman method, and optimization of its concentration would have constituted a known result effective variable within the purview of the skilled artisan.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure as general background information related to detection of homocysteine.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey R. Snay whose telephone number is (571) 272-1264. The examiner can normally be reached on Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey R. Snay
Primary Examiner
Art Unit 1743

jrs